PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference WESCX/P32619PC	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/GB2005/000592	International filing date *(day/month/year)* 18 February 2005 (18.02.2005)	Priority date *(day/month/year)* 21 February 2004 (21.02.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant WEST PHARMACEUTICAL SERVICES DRUG DELIVERY & CLINICAL RESEARCH CENTRE LTD		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 13 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 22 August 2006 (22.08.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Nora Lindner e-mail: pt02@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PP

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2005/000592	18.02.2005	21.02.2004

International Patent Classification (IPC) or both national classification and IPC
A61K47/36, A61K31/485

Applicant
WEST PHARMACEUTICAL SERVICES DRUG DELIVERY ...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2005/000592

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 32-35, with regard to industrial applicability

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 32-35, with regard to industrial applicability

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	6,12,13,31,35
	No: Claims	1-5,7-11,14-30,32-34
Inventive step (IS)	Yes: Claims	
	No: Claims	1-35
Industrial applicability (IA)	Yes: Claims	1-31
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III.

Claims 32-35 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V.

1
Reference is made to the following documents (for relevant passages see search report):

D1 : WO 02/40072 A (BIO SYNTECH CANADA INC; DESROSIERS, ERIC, ANDRE; CHENITE, ABDELLATIF;) 23 May 2002 (2002-05-23)

D2 : WO 01/36000 A (BIO SYNTECH CANADA, INC; CHENITE, ABDELLATIF; CHAPUT, CYRIL; WANG, DON) 25 May 2001 (2001-05-25)

D3 : US 2003/158302 A1 (CHAPUT CYRIC ET AL) 21 August 2003 (2003-08-21)

D4 : US 5 422 116 A (YEN ET AL) 6 June 1995 (1995-06-06)

D5 : HOFFMAN A S ET AL: "RELEASE OF CYTOKINE RECEPTORS FROM PHYSICAL HYDROGELS OF PLURONIC POLYETHERS GRAFTED TO CHITOSAN BACKBONES" PROCEEDINGS OF THE INTERNATIONAL SYMPOSIUM ON CONTROLLED RELEASE BIOACTIVE MATERIALS, vol. 24, 1997, pages 126-127, XP001029276 ISSN: 1022-0178

D6 : WO 96/03142 A (DANBIOSYST UK LIMITED; WATTS, PETER; ILLUM, LISBETH) 8 February 1996 (1996-02-08)

2
Document D1 discloses a composition comprising chitosan or derivative thereof and a beta-glycerolphosphate, gylcerol-2-phosphate or glucose-1-phosphate salt. Drugs may be

incorporated into the composition, as well as glycerol or polyethylene glycol, which are plasticisers. The composition turns into a gel within 20-70°C and the gel can be formed in situ in the eye.

2.1
INDEPENDENT CLAIM 1

As can be seen from the above, document D1 discloses in combination all the features defined in independent claim 1. Hence the subject-matter of this claim is not new (Article 33(2) PCT).

2.2
INDEPENDENT CLAIM 24

As can be seen from the above, document D1 discloses in combination all the features defined in independent claim 24. Hence the subject-matter of this claim is not new (Article 33(2) PCT).

2.3
INDEPENDENT CLAIM 25

As can be seen from the above, document D1 discloses in combination all the features defined in independent claim 25. Hence the subject-matter of this claim is not new (Article 33(2) PCT).

2.4
INDEPENDENT CLAIMS 26, 27, 28, 29, 32 AND 33

As can be seen from the above, document D1 discloses in combination all the features defined in independent claim 26. The same applies mutatis mutandis to the subject-matter

of independent claims 27, 28, 29, 32 and 33. Hence the subject-matter of these claims is not new (Article 33(2) PCT).

3

Document D2 discloses a composition comprising chitosan or derivative thereof and a beta-glycerolphosphate, gylcerol-2-phosphate or glucose-1-phosphate salt. Drugs may be incorporated into the composition, as well polyethylene oxide, which is considered to be a plasticizer. The composition turns into a gel within 10-70°C and can be used as an ophthalmological drug delivery system.

3.1

INDEPENDENT CLAIM 1

As can be seen from the above, document D2 discloses in combination all the features defined in independent claim 1. Hence the subject-matter of this claim is not new (Article 33(2) PCT).

3.2

INDEPENDENT CLAIM 24

As can be seen from the above, document D2 discloses in combination all the features defined in independent claim 24. Hence the subject-matter of this claim is not new (Article 33(2) PCT).

3.3

INDEPENDENT CLAIM 25

As can be seen from the above, document D2 discloses in combination all the features defined in independent claim 25. Hence the subject-matter of this claim is not new (Article

33(2) PCT).

3.4
INDEPENDENT CLAIMS 26, 27, 28, 29, 32 AND 33

As can be seen from the above, document D2 discloses in combination all the features defined in independent claim 26. The same applies mutatis mutandis to the subject-matter of independent claims 27, 28, 29, 32 and 33. Hence the subject-matter of these claims is not new (Article 33(2) PCT).

4
Document D3 discloses a composition comprising chitosan glycerophosphate, glucose-phosphate or fructose phosphate salts, polyethylene glycol or glycerol, and growth hormone or calcitonin. The composition forms gels at a temperature between 25-60 °C.

4.1
INDEPENDENT CLAIM 1

As can be seen from the above, document D3 discloses in combination all the features defined in independent claim 1. Hence the subject-matter of this claim is not new (Article 33(2) PCT).

4.2
INDEPENDENT CLAIM 24

As can be seen from the above, document D3 discloses in combination all the features defined in independent claim 24. Hence the subject-matter of this claim is not new (Article 33(2) PCT).

4.3

INDEPENDENT CLAIM 25

As can be seen from the above, document D3 discloses in combination all the features defined in independent claim 25. Hence the subject-matter of this claim is not new (Article 33(2) PCT).

5
INDEPENDENT CLAIMS 1, 24-29, 32 AND 33

All embodiments covered by the claims, particularly by the independent claims, should satisfy the criteria of inventive step (Article 33(3) PCT). The inventive step being based on the achievement of a technical effect, namely the provision a composition that initially has a low viscosity but that forms a gel at physiological temperature such that a gel is formed shortly after application to a mucosal surface, all the embodiments should exhibit this effect (see description page 2, lines 15-24). It must therefore be credible that all the alternatives claimed must be a solution to the problem.

It is clear from the comparative example iv, that the subject-matter of independent claims 1, 24-29, 32 and 33 does not exhibit a solution to the problem of the present application. In comparative example iv a solution containing chitosan glutamate 18.8 mg/mL, ß-glycerophosphate disodium 14.1 mg/mL and triethyl citrate 5 mg/mL had a solution viscosity of 173.7 cP, **which made the product unsuitable for dosing in vivo** (see description page 24, line 5).

Therefore, the subject-matter of claims 1, 24-29, 32 and 33 does not involve an inventive step (Article 33(3) PCT).

6
DEPENDENT CLAIMS 2-23, 30, 31, 34, 35

Dependent claims 2-23, 30, 31, 34, 35 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step (Article 33(2) and (3) PCT).
The reasons therefor are that the additional features of the said claims are either directly known from documents D1-D3, or are a combination of features obvious to the man skilled in the art in consideration of the disclosure of the prior art named in the present proceedings, i.e. D4-D6, or they concern only minor modifications which lie within the normal practice of the man skilled in the art.

7
For the assessment of the present claims 32-35 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VIII.

1
CLARITY

The application does not meet the requirements of Article 6 PCT, because claims 1, 3-5, 7, 8, 12, 26-29, 32 and 33 are not clear.

1.1
It is clear from the description on page 1, lines 1-2 and page 12, line 20 - last line and the comparative examples that the following features are essential to the definition of the invention:

(1) a therapeutic agent;
(2) compositions having a viscosity of 150 cP or less.

Since independent claim 1 does not contain feature (2), and independent claim 27 does not contain feature (1) they do not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.

1.2

The present application does not meet the requirements of Articles 6 PCT, because the term "derivative thereof, or a salt or derivative thereof" in claims 1, 7, 8 and 12 is unclear and the description does not provide any formula of derivatives of the claimed compounds.

1.3
Claims 3-5 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The following functional statements do not enable the skilled person to determine which technical features are necessary to perform the stated function: "which forms a gel at a temperature 30°C or greater", "which forms a gel in 15 minutes or less at a temperature of from 30 to 40°C", and "which forms a gel in 15 minutes or less at a temperature of from 35 to 37°C".

1.4
Although claims 26-29, 32 and 33 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.